## REMARKS

Upon entry of the amendment, claims 1-11 will be pending in the application. Support for the amendment to claim 1 appears in at the specification at, e.g., page 9, last paragraph. Claims 3, 6, 8, and 9 are amended to more particularly point out the subject matter claimed. No new matter is added. Claims 12-20 are cancelled in response to the Examiner's statement that they drawn to non-elected inventions. Applicants reserve the right to pursue the subject matter of all cancelled claims in a subsequent application or applications.

**Rejections under 35 USC § 102**

Claim 1 remains rejected as anticipated by Hill et al., J. Clin. Invest. 102:115-23, 1998 ("Hill") under 35 USC § 102(a). The rejection is traversed to the claim as amended.

The Examiner states:

> On page 8 of the specification, it is indicated that "immune-mediated disorder" means any disorder characterized by CTL and/or complement-mediated disorder. Furthermore, the specification indicates that IL-11 is administered to prevent immune-mediated disorder. Thus, preventing complement-mediated cytotoxicity is inherent to IL-11. Pretreating a mouse (mammal) with IL-11 prior to transplant will prevent complement-mediated cytotoxicity in said mammal. Therefore, the disclosure of Hill et al. anticipates instant claim 1.

The apparent basis of the Examiner's position is that any reference teaching administration of IL-11 to prevent any immune-mediated disorder inherently anticipates the claimed method complement mediated cytotoxicity. Applicants respectfully disagree.

Hill lacks any teaching of complement-mediated cytoxicity. Instead, it discusses the use of IL-11 in connection with Graft-Versus Host Disease (GVHD), a disorder mediated by cytotoxic T cell lymphocytes (see, e.g., Hill, Abstract). The latter is recognized in the specification and the prior art as an immune disorder much different than complement-mediated cytotoxicity.

For example, Applicants explain on page 9, second full paragraph of the specification, that complement action can proceed by a pathway based on antigen-antibody complex involving IgG or IgM, or an alternative pathway that can be activated by a bacterial endotoxin, polysaccharides, or complexes of antigen with other antibodies. In contrast, T-cell mediated graft-versus-host disease (GVHD) can occur when there are antigenic (in the case of organ transplants) differences in the MHC antigens between donor and recipient cells (see, e.g., paragraph bridging pages 1 and 2 of the specification). One treatment for GVHD described in the specification is to deplete immunocompetent donor T cells prior to transplantation (see page 2, first full paragraph of the specification).

The art additionally recognizes that cell-mediated lysis observed in cytotoxic T cell-mediated lysis is distinct from complement-mediated lysis. Hollander et al., J. Immunol. 142:3913-16, 1989, explain (page 3915, paragraph bridging columns 1 and 2, this reference is enclosed as Exhibit A):

> Distinct regulatory pathways for complement-mediated and cell-mediated cytolysis thus exist. This appears logical in view of the different functions of complement- and cell-mediated lysis The C [complement] system is critical for elimination of microorganisms. However, accidental attack of host cells by autologous C is undesirable and is prevented by C regulatory proteins present on the surface of host cells. Recognition is species-specific (homologous restriction). In contrast, cell-mediated cytotoxicity is critical for elimination of modified host cells. Resistance to autologous cell-mediated attack may therefore be disadvantageous.

Therefore, the art at the time Applicants' filed their application recognized that complement-mediated responses differ in fundamental ways from cell-mediated cytolytic immune responses. Thus, even if Hill were to be considered to teach a step that identifies a person in need of prevention of cell-mediated cytotoxicity, it does not follow that this reference inherently teaches Applicants' claimed step of identifying a mammal at risk of developing complement-mediated cytotoxicity. While Hill discusses the use of IL-11 to treat GVHD, which it describes as a T cell-mediated inflammatory process (see Abstract), this reference is silent about using IL-11 to treat complement-mediated disorders, let alone identifying a mammal at risk of developing complement-mediated cytotoxicity . Hill therefore fails to describe all the features of the claimed invention.

Applicants also disagree with the Examiner's use of their own specification in rejecting claim 1 as anticipated by Hill. While Applicants' disclosure teaches that IL-11 can be used to prevent either type of disorder, this teaching cannot be used by the Examiner to state that Hill therefore inherently the invention of claim 1. Applicants do not assert that these two types of disorders are identical, but are instead distinct species of the genus immune disorder. As is discussed above, the specification explains in detail how these disorders are mechanistically distinct. In short, the teachings of Hill, which is directed to the effects of IL-11 on a cytotoxic T cell mediated responses in GVHD, cannot be extrapolated to Applicants' method of reducing complement-mediated cytotoxicity.

Claim 6 remains rejected as anticipated under 35 USC § 102(b) by Yang et al, US Patent No. 5,700,664 ("Yang"). The rejection is traversed.

Claim 6 is drawn to a method of treating complement-mediated cytotoxicity in a mammal and requires both identifying a mammal with complement-mediated cytotoxicity and administering to the mammal a therapeutically effective amount of interleukin-11. Yang is cited for teaching the use of treating an immune-disorder using IL-11. However, this reference does not disclose that IL-11 can be used to treat complement-mediated cytotoxicity and more particularly fails to teach the claimed step of identifying a mammal with complement-mediated cytotoxicity. Therefore, it does not disclose all the features of the claimed invention and does not anticipate the claimed invention.

Reconsideration and withdrawal of the rejection for anticipation are respectfully requested.

**Rejections under 35 USC § 103(a)**

Claims 1-11 are rejected as obvious over Hill in view of Yang. The rejection is traversed.

Claims 1, 3, and 7, from which depend the remaining claims subject to the rejection, require identifying a mammal at risk for or having a complement-mediated cytotoxicity. Although the Examiner states that Hill and Yang teach preventing and/or treating complement mediated cytotoxicity (see paragraph 8 of the Office Action). Applicants respectfully disagree for the reasons explained above in their comments addressing the rejections under 35 USC § 102. Neither reference mentions complement-mediated cytotoxicity, nor is there any suggestion in either reference of administering IL-11 to a mammal that has been identified as at risk for, or suffering from, this type of disorder.

Moreover, as has been discussed above, the two pathways utilize different proteins and effect cell lysis in much different ways. In view of this distinction, there would have been no expectation that administering IL-11 to a mammal that has been identified as at risk for or suffering from this disorder would be successful

In view of the foregoing comments, reconsideration and withdrawal of the rejection for obviousness are requested.

**Rejection under 35 § USC 112, first paragraph**

Claims 1 and 2 are rejected for overbreadth. The rejection is traversed to the extent it is applied to claim 1 as amended.

Claim 1, from which depends claim 2, has been amended so that it is drawn to a method of reducing complement-mediated cytotoxicity. The Examiner acknowledges that the specification is enabled for using IL-11 to reduce complement mediated cytotoxicity (see paragraph 10 of the Office Action). Accordingly, the rejection is believed obviated by the amendment.

Reconsideration and withdrawal of the rejection are respectfully requested.

**Rejection under 35 § USC 112, second paragraph**

Claims 1, 3, and 6 are rejected as indefinite for reciting "identifying a mammal at risk for developing complement-mediated cytotoxicity or identifying a mammal with complement mediated cytotoxicity." The rejection is traversed.

The Examiner contends it is unclear how the mammal at risk is identified. However, the complement system has been extensively characterized (see, e.g., page 9, second full paragraph of the specification) and methods of determining the effects of complement action are well-known (see, e.g., Example 8 on page 22 of the specification). In addition, syndromes or conditions associated with complement-mediated cytotoxicity are known. Such diseases include, e.g., glomerular nephritis (see, e.g., Quigg et al., *Transgenic Mice Overexpressing the Complement Inhibitor Crry as a Soluble Protein Are Protected from Antibody-induced Glomerular Injury,* J. Exp. Med. 188:1321-31, 1998, enclosed as Exhibit B) and myocardial ischemia (see, e.g., Yasojima et al., *Human heart generates complement proteins that are upregulated and activated after myocardial infarction,* Circ. Res.19:860-69, 1998, enclosed as Exhibit C). In view of the teachings of the specification and the status of the prior art, Applicants submit that one of ordinary skill in the art can readily determine the metes and bounds of the claimed invention.

Reconsideration and withdrawal of the rejection are respectfully requested.

## CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for extension of time, accompanying fee, and information disclosure statement accompany this response. The Commissioner is hereby authorized to charge payment of any additional fees required in connection with the papers transmitted herewith, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 22058-521).

Respectfully submitted,

Dated: February 28, 2003

Ivor R. Elrifi, Reg. No. 39,529
David E. Johnson, Reg. No. 41,874
Attorneys for Applicants
MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241